STR SEARCH

Schnizer 09/627,787

L52 ANSWER 1 OF 33 HCAPLUS COPYRIGHT 2001 ACS
AN 2000:880999 HCAPLUS
DN 134:46793
TI Modification of biological elements by coating with multivalent polymers
IN Seymour, Leonard Charles William; Fisher, Kerry David
PA Cancer Research Campaign Technology Limited, UK
SO PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000074722	A2	20001214	WO 2000-GB2239	20000609
	WO 2000074722	A3	20010712		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI GB 1999-13359 A 19990609

AB A method of modifying the biol. and/or physicochem. properties of biol. elements such as viruses and other micro-organisms is disclosed in which the biol. element is modified by providing it with a coating of a multivalent polymer having multiple reactive groups. This modification can enable some biol. elements to be targeted or re-targeted to particular sites in a host biol. system and can be useful in connection with viral vectors for gene therapy or antitumor therapy. In other cases the modification can be useful for enhancing or improving the efficiency of viruses or bacterial micro-organisms used for example in pest control, degrdn. and dispersal of oil deposits and various other industrial, environment or medical applications. Concd. baculovirus particles (5x10⁸ particles/mL) in 100 .mu.L of PBS and 50 mM HEPES pH 7.4 were treated with 500 .mu.g of poly(N-2-hydroxypropylmethacrylamide)-Gly-Gly-ONp for 2 h on ice. For retargeting modified viruses, 10-100 .mu.g of targeting ligand (bFGF) was then added for a further 1 h. After that, 0.1% aminoethanol was added to complete reaction with any spare ester groups.

IT **100424-72-4P**
RL: AGR (Agricultural use); NUU (Nonbiological use, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(modification of biol. elements by coating with multivalent polymers for therapy, pest control and treatment of oil pollutions)

RN 100424-72-4 HCAPLUS
CN Glycine, N-(2-methyl-1-oxo-2-propenyl)glycyl-L-phenylalanyl-L-leucyl-, 4-nitrophenyl ester, polymer with N-(2-hydroxypropyl)-2-methyl-2-propenamide (9CI) (CA INDEX NAME)

CM 1

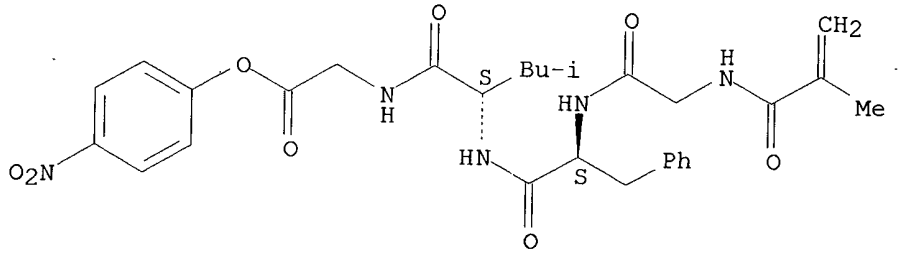
CRN 100424-71-3
CMF C29 H35 N5 O8

Searched by Paul Schulwitz

Schnizer 09/627,787

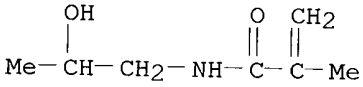
CDES 5:L,L

Absolute stereochemistry.



CM 2

CRN 21442-01-3
CMF C7 H13 N O2

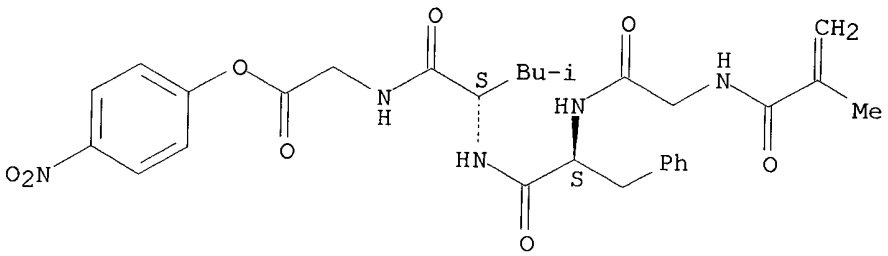


IT **312691-54-6P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(modification of biol. elements by coating with multivalent polymers for therapy, pest control and treatment of oil pollutions)
RN 312691-54-6 HCAPLUS
CN 2-5-Tachykinin-related peptide Ib (Cancer borealis), N-(2-methyl-1-oxo-2-propenyl)-, 4-nitrophenyl ester, polymer with N-(2-hydroxypropyl)-2-methyl-2-propenamide, graft (9CI) (CA INDEX NAME)

CM 1

CRN 100424-71-3
CMF C29 H35 N5 O8
CDES 5:L,L

Absolute stereochemistry.

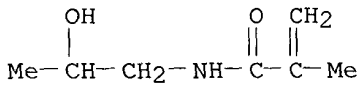


Searched by Paul Schulwitz

Schnizer 09/627,787

CM 2

CRN 21442-01-3
CMF C7 H13 N O2



L52 ANSWER 2 OF 33 HCAPLUS COPYRIGHT 2001 ACS
AN 2000:649039 HCAPLUS
DN 133:317302
TI Antiproliferative Effect of a Lectin- and Anti-Thy-1.2 Antibody-Targeted HPMA Copolymer-Bound Doxorubicin on Primary and Metastatic Human Colorectal Carcinoma and on Human Colorectal Carcinoma Transfected with the Mouse Thy-1.2 Gene
AU Rihova, B.; Jelinkova, M.; Strohalm, J.; St'astny, M.; Hovorka, O.; Plocova, D.; Kovar, M.; Draberova, L.; Ulbrich, K.
CS Institute of Microbiology, Academy of Sciences of the Czech Republic, Prague, 142 20, Czech Rep.
SO Bioconjugate Chem. (2000), 11(5), 664-673
CODEN: BCCHES; ISSN: 1043-1802
PB American Chemical Society
DT Journal
LA English
AB The aim of this study was to compare the potential of two plant lectins [peanut agglutinin (PNA) and wheat germ agglutinin (WGA)], monoclonal antibody (anti-Thy-1.2), its F(ab')2 fragments, and galactosamine as targeting moieties bound to the polymer drug carrier to deliver a xenobiotic, doxorubicin, to selected cancer cell lines. The authors have used primary (SW 480, HT 29) and metastatic (SW 620) human colorectal cancer cell lines and a transfectant, genetically engineered SW 620 cell line with mouse gene Thy-1.2 (SW 620/T) to test the possibility of marking human cancer with xenogeneic mouse gene and use it for effective site-specific targeting. The targeting moieties and doxorubicin were conjugated to a water-sol. copolymer based on N-(2-hydroxypropyl)methacrylamide (HPMA) acting as a carrier responsible for controlled intracellular release of the targeted drug. FACS anal. showed a strong binding of WGA-FITC to all tested cell lines. Binding of PNA-FITC was considerably weaker. The in vitro antiproliferative effect of lectin-targeted HPMA carrier-bound doxorubicin evaluated as [3H]TdR incorporation reflected both the intensity of the binding and the different sensitivity of the tested cancer cells lines to doxorubicin. The antiproliferative effect of conjugates targeted with WGA was comparable to that with the conjugates targeted with the anti-Thy-1.2 monoclonal antibody or their F(ab')2 fragments. The magnitude of the cytotoxic effect of HPMA-doxorubicin targeted with PNA was lower in all tested cell lines. While the conjugates with WGA were more cytotoxic, the conjugates with PNA were more specific as their binding is limited to cancer cells and to the sites of inflammation. Noncytotoxic conjugates with a very low concn. of doxorubicin and targeted with PNA, anti-Thy-1.2, or their F(ab')2 fragments exerted in some lines (SW 480, SW 620) low mitogenic activity. The Thy-1.2 gene-transfected SW 620 metastatic colorectal cancer cell line was sensitive to the antiproliferative effect

of Thy-1.2-targeted doxorubicin as was shown for the Thy-1.2+ EL4 cell line and for Thy-1.2+ Con A-stimulated mouse T lymphocytes. These results represent the first indication of the suitability of transfection of human cancer cells with selected targeting genes for site-specific therapy of malignancies.

IT **213338-45-5DP**, conjugates with doxorubicin and targeting moieties
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(antiproliferative effect of lectin- and anti-thy-1.2 antibody-targeted HPMA copolymer-bound doxorubicin on colorectal carcinoma in relation to **transfection** with thy-1.2 gene)

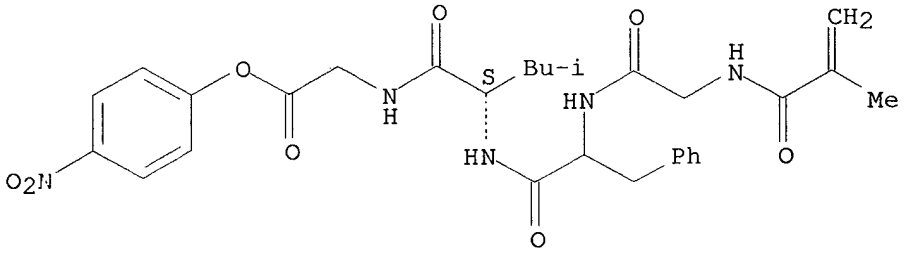
RN 213338-45-5 HCAPLUS

CN Glycine, N-(2-methyl-1-oxo-2-propenyl)glycylphenylalanyl-L-leucyl-, 4-nitrophenyl ester, polymer with 2-hydroxypropyl 2-methyl-2-propenoate (9CI) (CA INDEX NAME)

CM 1

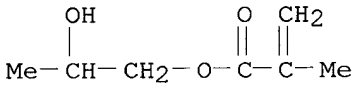
CRN 213338-44-4
CMF C29 H35 N5 O8

Absolute stereochemistry.



CM 2

CRN 923-26-2
CMF C7 H12 O3



RE.CNT 53
RE
(1) Bjorn, M; Cancer Res 1985, V45, P1214 HCAPLUS
(2) Boland, C; J Histochem Cytochem 1988, V36, P1305 HCAPLUS
(3) Buse, E; Histochem J 1998, V30, P819 HCAPLUS
(5) Chen, C; Mol Cell Biol 1987, V7, P2745 HCAPLUS
(9) Draberova, L; Eur J Immunol 1991, V21, P1583 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L52 ANSWER 3 OF 33 HCAPLUS COPYRIGHT 2001 ACS

Schnizer 09/627,787

AN 2000:129298 HCAPLUS
DN 132:330437
TI Decreased binding to proteins and cells of polymeric gene delivery vectors surface modified with a multivalent hydrophilic polymer and retargeting through attachment of transferrin
AU Dash, Philip R.; Read, Martin L.; Fisher, Kerry D.; Howard, Kenneth A.; Wolfert, Margreet; Oupicky, David; Subr, Vladimir; Strohalm, Jiri; Ulbrich, Karel; Seymour, Leonard W.
CS Cancer Research Campaign Institute for Cancer Studies, University of Birmingham, Birmingham, B15 2TA, UK
SO J. Biol. Chem. (2000), 275(6), 3793-3802
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
AB Binding of serum proteins to polyelectrolyte gene delivery complexes is thought to be an important factor limiting bloodstream circulation and restricting access to target tissues. Protein binding can also inhibit transfection activity in vitro. In this study a multivalent reactive hydrophilic polymer has been used to inhibit protein binding. This polymer is based on poly-[N-(2-hydroxypropyl)methacrylamide] (pHPMA) bearing pendent oligopeptide (Gly-Phe-Leu-Gly) side chains terminated in reactive 4-nitrophenoxy groups (8.6 mol%). The polymer reacts with the primary amino groups of poly(L-lysine) (pLL) and produces a hydrophilic coating on the surface of pLL.cntdot.DNA complexes (as measured by **fluorescamine**). The resulting pHPMA-coated complexes show a decreased surface charge (from +14 mV for pLL.cntdot.DNA complexes to -25 mV for pHPMA-modified complexes) as measured by .zeta. potential anal. The pHPMA-coated complexes also show a slightly increased av. diam. (approx. 90 nm compared with 60 nm for pLL.cntdot.DNA complexes) as viewed by at. force and transmission electron microscopy and around 100 nm as viewed by photon correlation spectroscopy. They are completely resistant to protein interaction, as detd. by turbidometry and SDS-polyacrylamide gel electrophoresis anal. of complexes isolated from plasma, and show significantly decreased nonspecific uptake into cells in vitro. Spare reactive ester groups can be used to conjugate targeting ligands (e.g. transferrin) on to the surface of the complex to provide a means of tissue-specific targeting and transfection. The properties of these complexes therefore make them promising candidates for targeted gene delivery, both in vitro and potentially in vivo.
IT **100424-72-4P**
RL: BUU (Biological use, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(pHPMA-ONp; decreased binding to proteins and cells of polymeric gene **delivery** vectors surface modified with multivalent hydrophilic polymer and retargeting through attachment of transferrin)
RN 100424-72-4 HCAPLUS
CN Glycine, N-(2-methyl-1-oxo-2-propenyl)glycyl-L-phenylalanyl-L-leucyl-, 4-nitrophenyl ester, polymer with N-(2-hydroxypropyl)-2-methyl-2-propenamide (9CI) (CA INDEX NAME)

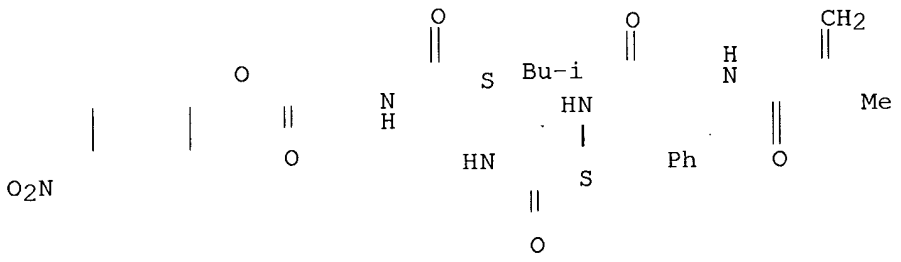
CM 1

CRN 100424-71-3
CMF C29 H35 N5 O8
CDES 5:L,L

Searched by Paul Schulwitz

Schnizer 09/627,787

Absolute stereochemistry.



CM 2

CRN 21442-01-3
CMF C7 H13 N O2

RE.CNT 26
RE
(1) Allen, T; Drugs 1998, V56, P747 HCAPLUS
(2) Anderson, W; Nature 1998, V392, P25 HCAPLUS
(3) Bonadio, J; Adv Drug Delivery Rev 1998, V33, P53 HCAPLUS
(4) Chao, J; Biodrugs 1999, V11, P43 HCAPLUS
(5) Dash, P; Gene Ther 1999, V6, P643 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L52 ANSWER 4 OF 33 HCAPLUS COPYRIGHT 2001 ACS
AN 1999:720562 HCAPLUS
DN 132:54713
TI Polymerizable Fab' antibody fragments for targeting of anticancer drugs
AU Lu, Zheng-Rong; Kopeckova, Pavla; Kopecek, Jindrich
CS Departments of Pharmaceutics and Pharmaceutical Chemistry/CCCD, and of Bioengineering, University of Utah, Salt Lake City, UT, 84112, USA
SO Nat. Biotechnol. (1999), 17(11), 1101-1104
CODEN: NABIF9; ISSN: 1087-0156
PB Nature America
DT Journal
LA English
AB We have designed a new pathway for the synthesis of targeted polymeric drug delivery systems, using polymerizable antibody Fab' fragments (MA-Fab'). The targeted systems can be directly prepd. by copolymn. of the MA-Fab', N-(2-hydroxypropyl)methacrylamide (HPMA) and drug-contg. monomers. Both MA-Fab' and the Fab'-targeted copolymers can effectively bind to target cells. An MA-Fab' (from OV-TL 16 Ab) targeted HPMA copolymer contg. mesochlorin e6 (Mce6) was synthesized by copolymn. of MA-Fab', HPMA, and MA-GFLG-Mce6. The targeted copolymer exhibited a higher cytotoxicity toward OVCAR-3 human ovarian carcinoma cells than the nontargeted Mce6-contg. copolymer or free Mce6. The targeted copolymer was internalized more efficiently by OVCAR-3 cells than the nontargeted